

REMARKS

Claims 1, 54, and 56 have been amended (i) to make it clear that the response which the integrated indicator structure exhibits is a response to being exposed to a condition and (ii) to incorporate the limitation of claim 5, that the condition be an environmental condition. Claim 5 has been amended to eliminate the redundancy introduced by this amendment to claim 1.

Claims 1, 3-10, 19-49, 54, 56, and 81-84 are under consideration.

The applicants thank the Examiner for withdrawing the section 112, first paragraph rejection of the previous Office Action.

The different objections and rejections are treated here in the order that they appear in the Office Action.

Objection to claim 82. The Examiner objects to claim 82 on the ground that it does not differ from claim 83. Claim 83 requires that the indicator structure be comprised of a double-stranded oligonucleotide having one labeled strand. Claim 82 requires that the indicator structure be comprised of a single-stranded oligonucleotide having defined sequences prehybridized to a labeled target. These claims are not precisely identical. For example, claim 83 requires that the labeled strand which has hybridized to the indicator be a target, whereas claim 82 does not contain any requirement that either strand of the double-stranded nucleotide be a target. For this reason, it is respectfully submitted that claim 82 and claim 83 may both properly be maintained.

Indefiniteness rejection of claims 81 and 84. Claim 81 is rejected as indefinite “because it is unclear as to the ability of the indicator structure to exhibit a response wherein the indicator structure is nucleotidic.” The Examiner asks, “what response is being ‘exhibit[ed]’ by a nucleotide when expose[d] to the condition and last[ing] for at least one minute after removing from the condition?” Nucleotidic materials (e.g., oligonucleotides and polynucleotides, single or double stranded) exhibit well-known responses to a variety of conditions such as temperature, pH, and the presence of reagents. They can, for example, denature or cross-link. Double-stranded oligo- and polynucleotides can dissociate to become single stranded. Single-stranded oligo- and polynucleotides can hybridize to become double stranded. Many of these responses are not reversible by removal of the condition; others, while reversible, may involve a return of the nucleotidic material to its prior state at a rate such that the response remains detectable for

one minute (or longer). In light of these facts, a person of skill in the art would understand what it means for a nucleotidic indicator structure to exhibit a response to being exposed to a condition. Claim 81 is not indefinite. For similar reasons, claim 84 is not indefinite.

Anticipation of claims 54 and 56 by Cargill. Cargill discloses oligomers which have “identifier tags.” The Examiner’s rejection of claims 54 and 56 over Cargill appears to be reading the claimed “integrated indicator” onto Cargill’s “identifier tag.” This read does not work with the claims as presently amended.

The integrated indicator must exhibit “a detectable response to being exposed to an environmental condition to which the device may be exposed” in claim 54 as currently amended. The integrated indicator must exhibit “a detectable response to being exposed to an environmental a condition” in claim 56 as currently amended. In contrast, in Cargill the identifier tag can be two things, as explained in considerable detail in part IV of Cargill’s detailed description, starting at column 21, line 23. First, the identifier tag can simply be a tag which says what the oligomer is and remains the same during the processes to which the oligomer is subjected. As such, the tag obviously does not respond to any conditions since it doesn’t change at all. Second, Cargill’s identifier can be a tag to which information is added as the oligomer is subject to processing, each addition being selected to reflect the processing that takes place. For example, in a preferred embodiment, the tag is a microchip into which the machine that is controlling the oligomers’ processing will write a record of what it is doing to them. Cargill col. 11, lines 3-7. The Cargill identifier tag consequently also does not respond to any environmental condition to which the device is exposed, but rather responds to information sent to the tag by the machine that controls the processing for recording in the tag.

To use an analogy, the Cargill identifier tag of the second type is like the medical record on a patient’s bed in a hospital, on which a nurse might write the patient’s temperature or other bodily condition as it is measured at different times. In contrast, the integrated indicator of the present claims itself reacts to the temperature or other condition, i.e., it is more like a thermometer which reacts to the patient’s temperature.

In sum, the Cargill tags do not exhibit “a detectable response to being exposed to an environmental condition” as required by claims 54 and 56 as currently amended. The Examiner’s read of the “integrated indicator” on the “identifier tag” of Cargill is thus not correct for the current claims, and rejections based on that read should be withdrawn.

Anticipation of claim 56 by Bioarray Solutions LLC. The Examiner's rejection of claim 56 over Bioarray Solutions LLC appears to be reading the claimed "integrated indicator" onto Bioarray Solutions' "color codes." This read does not work with the claims as presently amended.

The color codes of Bioarray Solutions have a role similar to the identifier tags of Cargill. They are a way to tag particular compounds in a combinatorial chemistry system. As Bioarray Solutions states, "[t]he color coding strategy of the present invention provides a method to place a set of fluorophores . . . on each bead so as to uniquely encode the chemical identity of the compound on that bead. Specifically, during each coupling step in the course of DCR combinatorial synthesis, one or more fluorophores are attached to each bead." Page 9, lines 16-20. Thus, the color codes do not respond to being exposed to an environmental condition as required by claim 56 as amended; rather, they are added deliberately to the beads as a way of recording what is done to the beads in the combinatorial synthesis process. See, e.g., Bioarray Solutions claim 1 (reciting carrying out a reaction with the beads in step b) and adding the color codes separately in step c)).

For these reasons, the Examiner's read of the "integrated indicator" on the "color codes" of Bioarray Solutions LLC is not correct, and rejections based on that read should be withdrawn.

Obviousness of claims 1, 3-10, 19-37, and 47-49 over Cargill and Wang. This obviousness rejection relies on the read of the "integrated indicator" on Cargill's "identifier tag." This is an inappropriate read as explained above. Therefore, the obviousness rejection should be withdrawn.

The Examiner did not include any specific reasoning for rejecting the dependent claims. Because each claim needs to be rejected separately, each claim being regarded as defining an invention, this does not meet the Examiner's burden to provide a basis for rejecting the claims.

In addition, in these obviousness rejections, the Examiner does not make it clear what the target recited in the claims being rejected is, nor where there is a disclosure of target-probe interaction in Cargill (or Wang for that matter). One possibility is that the Examiner is identifying the target recited in the claims with some substance which the combinatorial libraries of Cargill would react after synthesis, as described very briefly and in general terms in part VIII of Cargill. With this understanding, however, there is no specific disclosure in Cargill, for example, of the requirement of claim 5 that an environmental condition to which the indicator

structure responds allows for target-probe interaction, the requirement of claim 47 that “the targets represent portions of a single molecule” or the requirement of claim 48 that “the targets represent portions of single cell.” The rejections of those claims are incorrect for this independent reason.

Obviousness of claims 1, 6, and 81 over Brenner and Wang. The Examiner’s rejection of claims 1, 6, and 81 over Brenner and Wang appears to be reading the claimed “integrated indicator” onto Brenner’s “genetic tag.” This read does not work with the claims as presently amended.

Brenner’s genetic tag is an oligonucleotide attached to an oligomer. Its purpose, like that of the Bioarray color codes and the Cargill identifier tag, is to label the oligomer. Brenner’s idea is that (i) the oligonucleotide gets added to the oligomer when the oligomer is formed, and then (ii) the oligomer is tested somehow, e.g., in a receptor binding assay, and then (iii) when you want to know the structures of the oligomers which passed the test, you amplify and sequence their attached oligonucleotides. Brenner’s genetic tag is used to record what was done to build up the oligomer. Specifically, each time a monomer is added to the oligomer, an “alternating synthesis” is then used to add a short stretch of sequence to the oligonucleotide which represents the monomer which was added: “In each case, addition of a monomeric chemical unit to a polymeric structure is followed by addition of an oligonucleotide sequence which is defined as ‘encoding’ that chemical unit.” P. 5381, col. 2 bottom. Thus, the genetic tag does not respond to being exposed to an environmental condition to which the device is exposed, as required by claim 1 (and thus by claims 6 and 81 which depend on claim 1), but rather responds to a separate synthetic step.

Far from disclosing that the genetic tag responds to the environmental conditions to which the oligomers are exposed, Brenner expresses concern that the genetic tag remain *unchanged* under those conditions. Brenner states that “[t]he chemistry required for making encoded libraries is constrained only by the compatibility of the two alternating syntheses” (meaning the synthesis which adds the monomer to the oligomer and the synthesis which adds the short stretch of sequence to the oligonucleotide). “[E]ach product [oligomer and tag] needs to survive through the synthesis of the other.” P. 5383, col. 1.

In sum, because the read of the integrated indicator on Brenner's genetic tag is not correct for the current claims, the rejection of claims 1, 6, and 81 over Brenner and Wang should be withdrawn.

Examiner's response to applicants' arguments. The Examiner's response states that the claims do not require that "the indicator structure change during the course of the exposure to the condition," so that it is wrong of the applicants to distinguish prior art on the basis that it lacks such a feature. Irrespective of whether the claims formerly contained such a requirement, they have been amended to clearly contain such a requirement now; the integrated indicator structures must respond to being exposed to the condition.

The Examiner's response also states that, by pointing out that in prior art references information is added to the tags/color coding, the applicants are trying to read limitations into their claims which are not there. This is not the case. The applicants discuss that aspect of the prior art references merely to show that the changes undergone by the tags/color codes of the prior art reference are the result of the deliberate addition of information to the tags/color codes and not a response by the tags/color codes to a condition to which the device is exposed.

Allowable subject matter. At page 14 of the Office Action, the Examiner appears to be indicating that there is allowable subject matter in the claims. The Examiner's description of the allowable subject matter makes it sound like the subject matter of claim 83. While claim 83 is marked as rejected on the second page of the Office Action, it is believed that this was solely due to the indefiniteness rejection of claim 81 on which claim 83 depends, so that the subject matter of claim 83 is allowable. Confirmation would be very much appreciated.

In addition, while claims 38-46 are shown as being under consideration and rejected on the second page of the Office Action, there is no reasoning in the Office Action to justify rejecting them. The applicants would therefore appreciate the Examiner's indicating that their subject matter is allowable.

Conclusion

It is believed that the amendments made in this response place the claims in condition for allowance. It would be most appreciated if the Examiner would telephone the undersigned or send e-mail to rose@reedpatent.com if there is any question about this response.

Respectfully submitted,

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